

The response to Flexin in the present case was definite, but incomplete. Stiffness, subjectively evaluated, was less and no falls or dropping of objects occurred after administration of the drug was started. Balance in walking, originally very poor, was slightly better but was still poor. Objectively, there was no change in the muscles.

Flexin, a recently introduced mephenesin-like drug chemically unrelated to mephenesin, has been found to be of help in preventing or relieving spasm in voluntary muscles. The site of action is thought to be within the central nervous system upon polysynaptic pathways, where it causes depression with resultant relief of muscular spasm.<sup>3</sup> It is not believed to act upon muscle, the myoneural junction, motor nerves or monosynaptic reflex arcs. Use of it has been reported in rheumatic diseases,<sup>5</sup> in cerebral palsy<sup>1</sup> and in a variety of neurological disorders due to disease in either the brain or spinal cord.<sup>2</sup> A majority of the patients were appreciably helped. Patients with brain disorders were not helped as much as those with spasticity due to lesions of the upper motor neuron variety. Toxic reactions (chiefly gastrointestinal) generally were minor and all were reversible upon discontinuance of the drug.

### Successful Prochlorperazine Therapy Following Chlorpromazine-Induced Jaundice

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SINCE CHLORPROMAZINE came into general use by physicians in the United States in 1954, chlorpromazine-induced jaundice has been reported in a small number of patients.<sup>1-4</sup> Because of the structural similarity of chlorpromazine and prochlorperazine, and the fact that they are used in similar indications, the present case is of interest in that the patient became jaundiced when treated with chlorpromazine but was subsequently treated with prochlorperazine without complications.

#### REPORT OF A CASE

The patient, a 72-year-old white housewife, first observed December 23, 1955, had chronic bronchitis and a moderate anxiety state which was manifested in episodes of dizziness, fatigue, and "nervousness." Chlorpromazine, in daily doses of 25 mg., was administered orally for 11 days. The symptoms were dramatically relieved, and on January 4, 1956, a physical examination showed no significant abnormalities. Results of examination of the blood and urine and determination of serum protein were considered normal, and chlorpromazine therapy was discontinued.

The clinical history of the patient was of some interest. At the age of 17 she had had a stillborn infant at full term. Two spontaneous miscarriages, each

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#### SUMMARY

A case of "stiff-man" syndrome (progressive fluctuating muscular rigidity and spasm) in which treatment with Flexin was moderately helpful is reported.

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after about three months' gestation, followed. At age 26 a hysterectomy was performed for reasons unknown. Hemorrhoidectomy was done at age 57 without complications. Four years before the present illness, the patient had an attack of nausea, vomiting, and diarrhea of several weeks' duration, but this was not accompanied by jaundice and cleared up without specific treatment. She had always considered herself to be extremely nervous.

On January 11, 1956, the patient had an attack of nausea, vomiting, malaise and diarrhea. The temperature was 101° F. Cremomycin®\* and a bland diet were prescribed. In four days the temperature returned to normal.

By January 20 the gastrointestinal symptoms had abated, but in the afternoon of that day the temperature was 99.8° F. The patient had severe pruritus and definite jaundice. She was admitted to hospital in an acutely ill condition. The icteric index was 57 units, thymol turbidity 8 units. The result of a cephalin flocculation test was negative in 48 hours. The cell contents of the blood remained within normal limits. The urine was strongly positive for bile. Symptomatic treatment with fluids, a fat-free diet, Benadryl® (diphenhydramine hydrochloride) and mild sedatives was carried out but the patient did not improve.

On January 30 the icteric index was 63 units. Radiographs of the abdomen were considered normal, and a consultant recommended further observation and administration of steroids.

From February 1 to February 8 hydrocortisone was administered, 40 mg. four times daily, and from

\*Each 30 cc. contains: "Sulfasuxidine" succinylsulfathiazole, 3.0 gm.; colloidal kaolin, 3.0 gm.; pectin N.F., 0.3 gm.; neomycin sulfate, 300 mg.

February 8 to February 18, 20 mg. four times daily. Appetite and general health seemed to improve. The alkaline phosphatase, as determined during this time was 15 units and serum bilirubin 8 mg. per 100 cc. The cell content and protein levels in the blood were within normal limits. No abnormalities were noted in radiographs of the gastrointestinal tract.

On February 18 laparotomy was done. The liver was firm and blackish-green. The gallbladder and common bile duct were empty. Biopsy of specimens taken from the liver indicated a decided pericentral bile stasis within the intralobular bile capillaries and Kupffer cells. The bile canaliculi were filled with bile pigment. The central veins were not dilated, and there appeared to be little, if any, increase in the inflammation of the cells of the portal region. A few lymphocytes were present in the portal connective tissue, but there was no increase in the portal connective tissue itself. In one area a few lymphocytes were seen in the sinusoids of the liver. Other than bile stasis with some secondary changes in adjacent cells, no pathologic change was noted. The pathologic diagnosis was: Pronounced bile stasis of the liver, of unknown cause.

The patient recovered promptly from the operation and left the hospital a week later.

Loss of weight continued and icterus increased. The icteric index, as determined at monthly intervals, averaged 100 units. Pruritus was controlled fairly well with antihistamines, atropine and cold applications.

In July, large amounts of sugar were added to the diet. By coincidence or otherwise, jaundice began to clear, and a slow but progressive weight gain began. By the middle of October the patient appeared well and the results of laboratory examinations were within normal limits.

Later in the fall of 1956, episodes of nervousness similar to those that had occurred before were noted. Sedation and psychotherapy did not help. Some kind

of tranquilizing drug was felt to be indicated, but chlorpromazine was not considered because of the earlier chlorpromazine-induced jaundice. On November 26, 1956, prochlorperazine therapy was started after a thorough series of liver function studies. The drug was given from November 26 until November 30 in 5 mg. doses twice a day. The patient noted complete relief of all symptoms. At the request of the patient the dose was increased to 5 mg. three times a day, and this regimen was continued to January 28, 1957. Jaundice did not occur and repeated liver function tests showed no abnormalities.

#### SUMMARY

Severe jaundice occurred in a 72-year-old white woman nine days after discontinuance of chlorpromazine, which had been given for only a short time and in small amount. No beneficial results were observed when the patient was treated with steroids, but when large amounts of sugar were added to the diet, she promptly recovered. Prochlorperazine was administered a year later for the nervousness that had necessitated chlorpromazine. The patient was promptly relieved and then continued to take prochlorperazine for more than two months without evidence of hepatic damage.

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